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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/689,677 | 10/22/2003 | Neil M. Wolfman | 08702.0093-00000 | 2405 |

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| EXAMINER | |
|---|---|
| DUTT, ADITI | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1649 | |

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| 05/04/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/689,677 | WOLFMAN ET AL. | |
| | Examiner | Art Unit | |
| | Aditi Dutt | 1649 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *08 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-5,10-17,23,25,26,29-35,38 and 39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 10-17,23,29-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Status of Claims*

1. The amendment filed on 8 February 2007 has been entered into the record and has been fully considered. Claims 1, 3-5, 23, 38 and 39 are amended. Claims 6-9, 18-22, 24, 27-28, 36 and 37 are canceled.

2. Claims 1-5, 10-17, 23, 29-35, drawn to a method for increasing muscle mass in an individual with a disease or disorder requiring an increase in muscle mass, by administering a pharmaceutical composition comprising an Activin Receptor Type IIB (ActRIIB) fusion polypeptide comprising an amino acid sequence of at least 95% identical to amino acids 23-138 of SEQ ID NO: 3 and that is capable of binding to the growth and differentiation factor-8 (GDF-8), are under consideration in the instant application.

3. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicants response and withdrawn.

4. Applicant's arguments filed on 8 February 2007, have been fully considered. New grounds of objection and rejection are as follow.

***Response to Amendment***

Withdrawn objections and/or rejections

5. Upon consideration of the Applicant's amendment, all claim objections and rejections, not reiterated herein have been withdrawn, as overcome by cancellation and/or amendment of claims (8 February 2007).

6. Rejection of claims 1-5, 10-17, 23 and 29-37, under 35 U.S.C. 112, second paragraph is withdrawn, as a result of amendment of the claims.

35 USC § 112, first paragraph

Scope of Enablement

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. The rejections of claims 1-5, 10-17, 23 and 29-37, are applied to the amended claims 1-5, 10-17, 23, 29-35, for reasons of record in the Office Action dated 9 November 2006.

9. Applicant disagrees with the rejections set forth in the earlier Office Action, because Applicant believes that the specification has provided ample guidance with respect to the changes that can be introduced in the ActRIIB polypeptide sequence to obtain 95% homology to amino acids 23-138 of SEQ ID NO: 3, without disturbing the binding properties to GDF-8. Applicant asserts that requisite guidelines are presented for the production of different variants that can

retain GDF-8 binding activity. Based on the disclosure and the knowledge in the art, Applicant argues that selection of sequences having 95-99% identity by routine sequencing, measuring the binding activity by routine binding assays, could constitute simply routine, not undue experimentation. Applicant cites case laws to assert this contention, thereby requesting the withdrawal of the enablement rejection.

10. Applicant's arguments have been fully considered but have been found to be persuasive in part. Based on the Applicant's arguments and the clarification of the guidance provided in the disclosure, the rejection based on 95% to 99% sequence identity to amino acids 23 to138 of SEQ ID NO: 3 is withdrawn. Thus, the specification is now enabled for increasing muscle mass as exemplified in Example 9 (pages 46-47), via administration of ActRIIB-Fc (type II activin receptor B) fusion protein or its variants having 95% to 99% sequence identity to amino acids 23 to 138 of SEQ ID NO: 3, however, does not reasonably provide enablement for increasing of muscle mass in an individual with any disorder, for example Duchenne's muscular dystrophy (DMD). Applicant amended the claims to recite a method for increasing the muscle mass in an individual with any disease, requiring such increase, for example as in DMD. As the amended claims still recite Duchenne's muscular dystrophy, and because Applicants have not used the right animal model for studying increasing muscle mass in DMD, the rejections as described earlier are applied to the amended claims, for reasons explained in the previous Office Action (page 8-9, para 15-16).

11. Specifically, proper analysis of the Wands factors was provided in the previous Office Action. Due to the large quantity of experimentation necessary to treat increase in muscle mass in any disorder; the lack of direction/guidance presented in the specification regarding the same; the complex nature of the invention; the unpredictability of administering the fusion peptide in vivo and the state of the prior art which establishes the utilization of the animal models to study/treat DMD - undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

Written Description

12. The rejections of claims 1-5, 10-17, 23 and 29-37, are applied to the amended claims 1-5, 10-17, 23, 29-35, for reasons of record in the Office Action dated 9 November 2006.

13. Applicant argues that the recited polypeptides in the instant specification exceeds the written description requirement as stated in USPTO's Written Description Guidelines (Example 14), because the claims related to the polypeptide satisfy structural and functional limitations (95-99% identity and having GDF-8 binding activity), required for written description compliance. Applicant also argues that the specification provides both structure and physical properties of the claimed genus.

14. Applicant's arguments have been fully considered but have been found to be persuasive in part, for reasons explained above. The written description

requirement for variants is thus withdrawn. However, as stated in the previous Office Action (pages 11-13),

> The brief description in the specification of one example of increasing skeletal muscle weights in C57B6/SCID mice, is not adequate written description of an entire genus of methods encompassing a genus of muscle degenerative disorders associated with GDF-8.
>
> The specification has not shown adequate identifying characteristics of the claimed genus of degenerative disorders. Therefore, only methods of increasing skeletal muscle mass in muscular dystrophy, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph.

***Status of Claims***

15. No claims are allowed.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

17. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will

the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aditi Dutt whose telephone number is (571) 272-9037. The examiner can normally be reached on Monday through Friday, 9:00 a.m. to 5:00 p.m.

19. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

20. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov/. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

AD

13 April 2007

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER